Atypical carcinoid tumour of the larynx treated with CO_2 laser excision: case report

Un caso di carcinoide atipico laringeo trattato mediante exeresi con laser CO_2

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Key words

Tumours of the larynx • Neuroendocrine tumours • Surgical treatment • Laser CO_2 • Case report

Parole chiave

Tumori della laringe • Tumori neuroendocrini • Terapia chirurgica • Laser CO_2 • Caso clinico

Summary

A case of atypical laryngeal carcinoid tumour of the right aryepiglottic fold is described in a 56-year-old female. The patient presented a 4-year history of dysphagia, occasional dyspnoea and pain originating in the right tonsillar fossa and radiating to the ear. A sessile, submucosal neoplasm of about 1 cm in diameter and apparently benign appearance was detected endoscopically in the supraglottic region. An excisional biopsy was collected by CO_2 laser during direct microlaryngoscopy from which a diagnosis of atypical carcinoid tumour of the larynx was made, and later confirmed by histochemical and immunohistochemical staining. Post-operative course was uneventful, with return to a normal diet per os on the first post-operative day. Histopathological evaluation of the excised specimen revealed the presence of a neoplasm in proximity of the surgical margins, which were not, however, directly involved by the tumour. The close endoscopic follow-up was, nonetheless, implemented in order to promptly detect any evidence of relapse of the disease. After 18 months, a lesion, suspected of being a recurrence, was found, in the site of the original tumour. CO_2 laser excision was again carried out, this time allowing for wider margins on the surgical resection. The post-operative diagnosis confirmed the clinical hypothesis of recurrence of atypical carcinoid tumour. The patient is presently alive and free from disease 7 years after the second endoscopic procedure. The difficult aspects of clinical and histopathological diagnoses, the surgical treatment as well as endoscopic and instrumental follow-up of this rare condition are discussed.

Riassunto

Viene descritto un caso di carcinoide atipico laringeo della plica ariepiglottica destra in una donna di 56 anni. La Paziente presentava da circa 4 anni una sintomatologia caratterizzata da disfagia, dispnea occasionale e dolore a partenza dalla loggia tonsillare destra, irradiato all'orecchio. Endoscopicamente venne identificata in regione sovraglottica una neoformazione sessile, sottomucosa, di circa 1 cm di diametro ed aspetto apparentemente benigno. Una biopsia escissionale in microlaringoscopia diretta mediante laser CO_2 consentì di porre la diagnosi, poi confermata da colorazioni istochimiche ed immunoistochimiche, di carcinoide atipico laringeo. Il decorso postoperatorio si svolse senza complicanze di sorta, con ripresa di una normale alimentazione per os in prima giornata. La valutazione istopatologica del pezzo operatorio dimostrò la presenza di neoplasia in prossimità dei margini di resezione chirurgici, senza un loro diretto coinvolgimento da parte del tumore. Uno stretto controllo endoscopico venne comunque eseguito per evidenziare precocemente ogni eventuale segno di ripresa della malattia. Dopo 18 mesi venne riscontrata, in corrispondenza della sede del tumore primitivo, una lesione sospetta per recidiva. Questa venne nuovamente trattata mediante exeresi con laser CO_2, provvedendo questa volta ad ottenere margini più ampi di resezione chirurgica. La diagnosi postoperatoria confermò l'ipotesi clinica di una recidiva di carcinoide atipico. La paziente è attualmente viva e libera da malattia a 7 anni dal secondo intervento endoscopico. Vengono quindi discusse le problematiche nella diagnosi clinica ed istopatologica, nel trattamento chirurgico e nel follow-up endoscopico e strumentale di questa rara entità nosologica.

Introduction

The latest classification of tumours of the upper respiratory tract edited by the World Health Organisation [1] divides neuroendocrine neoplasms of the larynx into two types: epithelial and nervous. The latter is represented by paragangliomas alone, while the former includes both the typical and the atypical carcinoid tumour (ACT), also called small-cell neuroendocrine carcinoma. This last oncotype may be further distinguished in oatmeal cell carcinoma, intermediate cell carcinoma and mixed cell carcinoma.

Neuroendocrine tumours are the most common non-squamous cell neoplasms of the larynx, with over 500 cases being reported in the international literature. Atypical laryngeal carcinoid tumour (ALCT)

accounts for approximately 50% of these tumours [2]. A case of ACT treated with CO_2 laser excision during direct microlayngoscopy is described.

Clinical case

In December 1993, a 56-year-old female was hospitalised in the Otorhinolaryngology Clinic of the University of Brescia with dysphagia, occasional dyspnoea and pain in the area of the right tonsillar fossa, radiating to the homolateral ear. Symptoms had been present for 4 years and the patient had previously been diagnosed elsewhere as affected by idiopathic neuralgia of the glossopharyngeus. Laryngoscopy, instead, revealed the presence of a neoplasm of the right aryepiglottic fold, about 1 cm in diameter, greyish-white in colour, sessile, submucosal and with scarse superficial telangiectases. The most feasible working diagnosis seemed that of a polyp or laryngeal granuloma arising in an atypical site, the appearance of which was, however, fundamentally benign. The remainder of the objective examination, routine blood tests and a chest X-ray were, furthermore, all normal.

In order to offer an explanation for the symptoms referred by the patient, it was decided to carry out endoscopic excision via CO_2 laser given the feasibility of a direct laryngoscopical surgical procedure and the benign macroscopic appearance of the neoplasm (Fig. 1). The, as yet, unknown histopathological nature of the nodule suggested a minimal, ultraconservative approach, without seeking to leave particularly wide margins around the lesion; under the surgical microscope, the latter appeared to be free from neoplasms and, therefore, no intraoperative frozen section was made. In the course of surgery, however, the surgeon (G.P.) noticed that the mass was characterised by an enhanced texture and by an abnormal pattern both in the superficial and deep vascular distribution, hardly compatible with the diagnosis of a polyp or granuloma initially formulated on the basis of an exclusively endoscopic assessment.

There were, however, no post-operative complications and the patient was discharged on the first post-operative day, on a normal diet per os.

The definitive histopathological diagnosis, on the excised tissue, was ACT of the larynx. The microscopic evaluation, in fact, showed the presence of neoplastic cells of fusiform appearance, with moderately hyperchromic nuclei, prominent nucleoli, eosinophilic cytoplasm and scarse mitosis. The tumour cells presented a nest-like trabeculate organisation, with cribriform-patterned foci (Fig. 2). There was also marked vascular invasion, and Grimelius staining revealed intensely argyrophilic cytoplasm granules. Histochemical and immunohistochemical staining detected diffuse positivity to calcitonin (Fig. 3), chromogranin A, CAM-5.2, focal positivity for CEA and PGP-9.5. On the contrary, staining for S-100 protein, NSE and NFP were negative. The surgical margins of the resection, although very close, were, albeit, free from neoplastic involvement and treatment was considered complete.

Endoscopic follow-up was performed every 2 months by means of rigid laryngoscopy (70° scope), associated once yearly with magnetic resonance of the head and neck, chest X-ray, bone scintigraphy

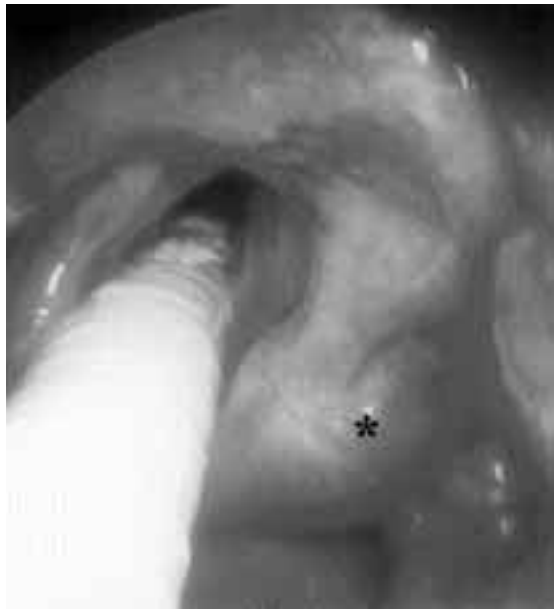

Fig. 1. Intraoperative endoscopic appearance of ALCT in right aryepiglottic fold (asterisk).

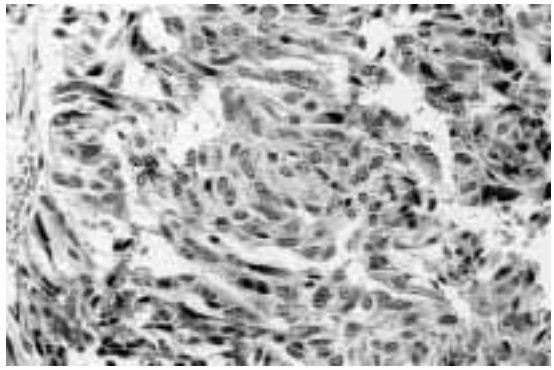

Fig. 2. Histopathological pattern of ALCT (H&E, magn x 20).

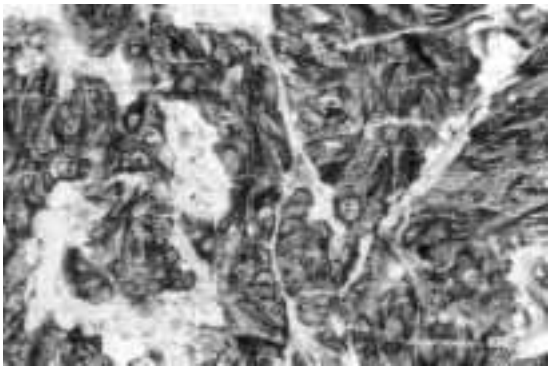

Fig. 3. Immunohistochemical study of lesion with calcitonin (magn x 40).

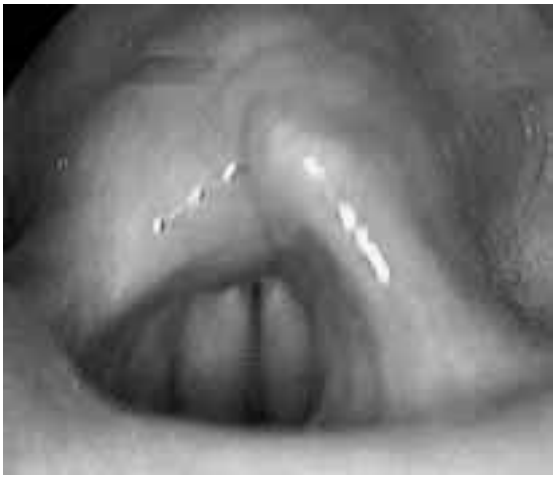

Fig. 4. Videolaryngostroboscopic evaluation 7 years after treatment of recurrence.

and echography of the liver and neck.
Eighteen months after the procedure, endoscopy revealed a suspected recurrence of the neoplasm in the same laryngeal subsite as the original tumour. The new lesion, similar in size and appearance to the previous one, was treated with CO_2 laser during a second direct microlaryngoscopy. This time, however, every attempt was made to achieve wider surgical margins in healthy tissue. No suspicious lymphadenopathy was observed upon laterocervical echography, nor were any distant metastases detected upon complete radiological evaluation of the patient. The definitive histopathological examination confirmed both the diagnosis of ACT made after the first operation and the absence of neoplastic infiltration or proximity of the neoplasm to the surgical margins. At the last endoscopic check-up (Fig. 4) and radiological MR evaluation, the patient, completely asymptomatic, was free from disease 7 years after treatment of the recurrence.

Discussion

95% of ALCT of the larynx originate in the supraglottic region and favour males in their sixth-to-seventh decade of life. The most common symptoms are dysphonia, dysphagia, dyspnoea, odynophagia and secondary neuralgia of the glossopharyngeus. This last symptom, in particular, has often been present for several years prior to diagnosis, as in the case described here. The ACT paraneoplastic syndrome is, instead, a clinical finding, rarely associated with ACTs of the larynx.
Macroscopically, this neoplasm is usually constituted by a polypoid mass, pedunculated or nodular, submucosal, at times with evident superficial mucosal erosions. In the absence of mucosal ulceration, the macroscopic appearance of ACTs is completely compatible with that of a benign lesion.
The histopathological diagnosis is based on routine microscopy, but histochemical, immunohistochemical and ultrastructural examinations under the electron microscope are often required. The differential diagnosis must essentially be made versus other types of neuroendocrine neoplasms, with particular attention to paragangliomas [3 4].
Appropriate treatment of an ACT of the larynx, in its initial stage, may undoubtedly include endoscopic surgery, although, in the case of apparently benign-looking lesions, like the one described here, there is always the problem of having to decide when to effect a resection with wide margins in healthy tissue. This becomes particularly important in several subsites of the larynx, as, for example, the glottis, where dysfunctional sequelae are strictly correlated to the quantity of tissue removed. Albeit, the best decisional criterion appears to be determined by accurate evaluation of the symptoms and careful examination of the lesion under the surgical microscope. In dubious cases, intraoperative frozen section should be carried out. Should a post-operative diagnosis of ALCT be made following definitive examination of the specimen excised, two attitudes are, in our opinion, equally justified: either strict routine endoscopic follow-up enabling a prompt diagnosis to be made in the event of local recurrence, or prompt reoperation, in order to achieve wider resection margins.
Neck lymph nodes should be excised only when there is clinical suspicion or radiological evidence of a metastasis of the neoplasm at latero-cervical level. In these cases, the surgical approach to the original tumour will, consequently, also be planned taking in-

to consideration treatment of regional metastasis, as well as, obviously, the size and local extension of the tumour.

The results reported in the literature in which radiotherapy and chemotherapy have been employed still remain uncertain and controversial [5]. Regardless of the choice of treatment for the original tumour, in fact, the regional and distant metastases, often already present upon diagnosis, remain the principal cause of death in ALCT, the prognosis of which is, therefore, generally dismal and fundamentally independent of the treatment carried out on the original tumour. The overall survival rates reported range from 48% at 5 years to 30% at 10 years [6]. The size of the tumour is considered by many Authors, an important prognostic predictor, with mortality rates doubling in patients in whom neoplasms >1 cm [6-8].

In the presence of small-sized ALCTs, carefully selected so as to exclude neoplastic infiltration of deep laryngeal structures and spaces, CO_2 laser excision during endoscopy, as in the present case, combined with a strict echographic follow-up of the neck, may be considered a valid alternative to the traditional cervicotomic surgical approach. In our experience, in fact, recurrence, after the first endoscopic procedure, is likely due to the ultraconservative approach adopted in the absence of a preoperative histopathological diagnosis as well as the aspecific appearance of the lesion itself. A strict, long-term follow-up is indispensable for the early detection of any local recurrence, which may, when possible, be submitted to further endoscopic treatment keeping wider excision margins.

In conclusion, the low morbility, good quality of life and favourable cost/benefit ratio, associated with good local control obtained by means of the endoscopic procedure during direct microlaryngoscopy, play an important role in the choice of treatment even for ALCTs in the initial stage. If, in fact, prognosis of these neoplasms depends substantially upon the lymph nodes and distant metastases, once the presence of the latter has been excluded, the treatment of the original tumour is based on a simple criterion of size, with lesions approximately 1 cm in diameter being easily excised by means of an endoscopic approach. Since a high rate of metastases is common in this type of neoplasm, however, radiological evaluation, at regular intervals, is mandatory in order to promptly reveal and treat any secondary localisations.

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